510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
K033487

B. Analyte:
Troponin I

C. Type of Test:
Quantitative sandwich fluorometric immunoassay

D. Applicant:
Dade Behring, Inc.

E. Proprietary and Established Names:
Stratus® CS Acute Care™ Troponin I assay

F. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1215, Creatine phosphokinase/creatine kinase or isoenzymes test system
2. Classification:
   Class II
3. Product Code:
   MMI, Creatine phosphokinase/creatine kinase or isoenzymes test system
4. Panel:
   Clinical Chemistry (75)

G. Intended Use:

1. Indication(s) for use:

The Stratus® CS Acute Care™ Troponin I method is an in vitro diagnostic test for the measurement of cardiac Troponin I in heparinized plasma. Cardiac Troponin I measurements can be used as an aid in the diagnosis of myocardial infarction. Cardiac Troponin I can also be used as an aid in the risk stratification of patients with acute coronary syndromes with respect to their relative risk of mortality.

2. Special condition for use statement(s):

For professional use only.

3. Special instrument Requirements:

Dade Stratus® CS STS Fluorometric Analyzer

H. Device Description:

The Stratus® CS Acute Care™ Troponin I assay is a sandwich-type immunofluorometric assay which consists of a test pack containing two wet reagents that each contain buffers and distinct anti-Troponin I antibodies, wash buffer that contains indicator substrate, and a glass fiber paper substrate. One of the antibodies is dendrimer linked (for immobilization on the glass fiber paper) and the other antibody is linked to alkaline phosphatase (indicator).

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Stratus® CS STAT cardiac Troponin I assay
2. Predicate K number(s):
   K984093
   K981098
3. Comparison with predicate:

The 510(k) is for labeling changes only. No changes to the process or formulation were made, so the device is identical in intended use and performance characteristics. Changes to the labeling are indicated below.

Item	Revised Insert Sheet Change
Method Name	Stratus® CS Acute Care™ Troponin I (formerly the Stratus® CS cTnI TestPak)
Test Steps	Clarification of steps performed automatically allowed removal of Results section
Interpretation of results	1. Added National Academy of Clinical Biochemistry statement 2. Added statement on results interpretation in conjunction with medical history 3. Moved some statements from the Diagnosis of AMI section 4. Added statements on institutions establishing own reference interval and other conditions which can lead to myocardial injury
Reference interval	Presentation of 97.5th and 99th percentile results instead of the 95th percentile
Risk Stratification	Added American College of Cardiology (ACC)/AHA definition for short term risk of death/non-fatal MI
Diagnosis of AMI	1. Added sensitivity/specificity graph 2. Added EU Society of Cardiology/ACC statement on MI definition 3. Added functional sensitivity information at the 99th percentile

Performance Characteristics	Added plasma pool reproducibility data
Correlation Data	Added performance comparison versus Dade Behring Dimension® clinical chemistry system
Recovery	Clarified titles in charts
Bibliography	Added references

J. Standard/Guidance Document Referenced (if applicable):
None referenced.

K. Test Principle:
In the automated analyzer, the dendrimer-linked monoclonal anti-TnI antibody is first immobilized on the glass fiber paper. Sample is then added and incubated to allow for binding of TnI in the sample to the antibody. The second antibody solution (alkaline phosphatase-labeled) is then added which binds a separate site on the TnI molecule. The spot is washed with a solution that also contains the enzyme substrate thus initiating the indicator reaction and washing the unbound antibody away. The enzymatic rate of the reaction increases directly with increasing Troponin I concentration.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:
    a. Precision/Reproducibility:

Low end assay imprecision was tested to determine if this assay meets the recommended criteria for a high sensitivity troponin test (Joint Committee of the ESC/ACC recommendation of 10% imprecision at the 99th percentile of normal). Nine plasma pools (site 1) and 5 plasma pools (site 2) with troponin concentrations ranging from 0.04 to 0.40 ng/mL were assayed in duplicate once a day on each of two analyzers for 20 days. A negative sample was also assayed as well as a commercial control. The data is summarized below (ng/mL).

Sample	Target Value	Grand Mean	SD	% CV
Pool 04	0.04	0.04	0.006	16.2
Pool 09	0.09	0.08	0.006	7.45
Pool 2	0.2	0.17	0.007	4.14
Pool 4	0.4	0.33	0.11	3.46
Pool 6	0.6	0.58	0.19	3.29
L0	0	0.002	0.005	269.7
L1	0.3	0.347	0.012	3.54
L2	0.2	0.212	0.009	4.04
L3	0.1	0.12	0.007	5.98

L4	0.06	0.065	0.006	9.69
L5	0.04	0.04	0.006	14.6
L5B	0.04	0.038	0.006	16.2
L6	0.05	0.052	0.007	14.2
L6B	0.05	0.053	0.007	13.9
L7	0.01	0.007	0.006	91.4
Control	0.6	0.645	0.025	3.86

b. Linearity/assay reportable range:

Not applicable. The performance characteristics and the process are not changed in this submission. Please refer to the predicate submissions for performance data.

c. Traceability (controls, calibrators, or method):

Not applicable. The performance characteristics and the process are not changed in this submission. Please refer to the predicate submissions for performance data.

d. Detection limit:

This device meets the standard recommended by the Joint Committee of the European Society of Cardiology/American College of Cardiology for a high sensitivity Troponin test. This assay has ≤10% imprecision (%CV) at the 99th percentile of normals (0.07 ng/mL).

e. Analytical specificity:

Not applicable. The performance characteristics and the process are not changed in this submission. Please refer to the predicate submissions for performance data.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor added information comparing the device to another commercially available device. 168 patient samples ranging from 0.0 to 34.38 ng/mL were assayed in singleton on each device. The following regression equation resulted:

$y = 0.96x - 0.11$, $r = 0.99$

b. Matrix comparison:

Not applicable. The performance characteristics and the process are not changed in this submission. Please refer to the predicate submissions for performance data.

3. Clinical studies:

a. Clinical sensitivity:

The sponsor has added a graph to the labeling that shows sensitivity and specificity at cutoff concentrations ranging from 0.6 to 1.65 ng/mL Troponin I. This figure is supported by studies from the sponsor's files. 314 patients presenting with chest pain to the ER (3 study sites) were evaluated for AMI by WHO criteria (chest pain, ECG changes, and cardiac marker changes). For each patient, troponin I was measured in three serial samples. A positive troponin I result was recorded if any one of the three serial specimens taken in a 24 hour period was equal to or exceeding the cutoff being evaluated. A result was considered negative if all three serial samples were below the cutoff being evaluated. The troponin result was evaluated against clinical diagnosis. The results were as follows:

cTnI cutoff (ng/mL)	Sensitivity	Specificity
0.60	94.5 %	96.2 %
0.75	94.5 %	96.8 %
0.90	94.5 %	97.3 %
1.05	93.8 %	97.3 %
1.20	93.0 %	98.4 %
1.35	93.0 %	98.9 %
1.50	93.0 %	98.9 %
1.65	92.2 %	98.9 %

b. Clinical specificity:

See clinical sensitivity section above.

c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:

See clinical sensitivity section above for information about potential cutoff concentrations. The sponsor states that cutoffs between 0.6 and 1.65 are consistent with WHO criteria for AMI.

5. Expected values/Reference range:

The sponsor established their Troponin I reference range for normals by testing 101 apparently healthy individuals using their device. The 97.5^{th} percentile is reported as 0.00 to 0.06 ng/mL and the 99^{th} percentile is reported as 0.00 to 0.07 ng/mL. Users are cautioned to establish reference intervals appropriate for their institution and patient population.

M. Conclusion:

I recommend that the Stratus® CS Acute Care™ Troponin I assay is substantially equivalent to the legally marketed predicate device.